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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/579,894	05/26/2000	Kalle Saksela	0933-0159P	9956

2292 7590 08/26/2003

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EXAMINER

CELSA, BENNETT M

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 08/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

file COPY

Office Action Summary

Application No.

09/579,894

Applicant(s)

Saskela et al.

Examiner

Bennett Celsa

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jun 16, 2003
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above, claim(s) 5-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 17-19 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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Status of the Claims

Claims 1-19 are currently pending.

Claims 1-4 and 17-19 are under consideration.

Claims 5-16 are withdrawn from consideration as being directed to nonelected subject matter. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Withdrawn Objection (s) and/or Rejection (s)

Applicant's amendment has overcome the indefinite rejection of claim 17 presented in the prior office action.

Outstanding Objection(s) and/or Rejection (s)

1. Claims 1-4 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Lee et al. Embo J. Vol. 14, No. 20 pages 5006-5015 (1995)..

Lee et al. discloses a method of producing SH3 domains from the RT-loop region of different SH3 domains (e.g. from different SH3-kinases). Lee produces said SH3 domains by first mutating some residues of the RT-loop of the different SH3 domains, e.g. page 5010, Fig. 4. The "collection" of mutant RT-loop region is obtained from a library of cDNA (e.g. a collection of 2 or more). "DNA fragments encoding" SH3 domains containing a "randomized RT-loop (RRT-SH3 domains)" are taught by the reference e.g. by use of cDNA encoding the kinase (e.g. human Hck) and polymerase chain reaction (e.g. amplification using primers) with "cloning"

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utilizing a “plasmid *vector*” to generate the recombinant library (e.g. see Lee et al. page 5013, right column). The RT-loop mutated region is then affinity purified to identify the mutant RT-loop peptide that binds to the PXXP motif of a ligand (e.g., Nef) *with higher specificity and affinity* than the corresponding wild -type SH3 domain ; as well as the binding of the other “artificial” (e.g. unnaturally occurring) SH3 domains to their “desired ligands”. In this regard the reference discloses “randomized” substitutions (one or a *combination e.g. 2, 3*) of amino acid substitutions within the RT loop, and specifically within non-conserved (e.g. “variable” regions), and *preferably* including one or more substitutions (e.g. within a specific kinase or among a library of kinases) within a span which “*comprise* six amino acids that immediately follow a conserved stretch of amino acids having an ALYDY consensus sequence”. [See e.g. Fig. 4 teaching both conserved and non-conserved amino acids of the RT-loop of kinases and Table I teaching the construction of a library (e.g a collection) of different kinases having “artificial SH3 domains having desired ligand binding properties” “comprising randomized RT-loops” wherein the collection of SH3 domains contain one or more “random” amino acid substitutions that comprise a hexapeptide sequence “that immediately follows a conserved stretch of amino acids having an ALYDY” (e.g. ...(AL) YDY . hexapeptide DLS ...]. With respect to SH3 binding and specificity (e.g. w/r to differential binding of SH3 containing kinases e.g. Hck and Fyn) to HIV-I, the Lee reference teaches that “**distinct specificity lies in a variable loop, the ‘RT loop’, positioned close to conserved SH3 residues implicated in the binding of proline-rich (PXXP) motifs**” (emphasis provided) . See ABSTRACT. It is considered that the different

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mutations of the different SH3 regions of the different kinases is the same to the claimed randomized RT-loop domains or would have been obvious to make into a random collections in view of the Lee's disclosure as to the different amino acids that can be mutated in the different SH3 domains of the SH3 wild type, particularly within the non-conserved regions of the RT-loop motif.

Discussion

Applicant's amendment and arguments relating to the above 102/103 rejection was considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above 102/103 rejection was modified in order to address the newly amended claim limitations.

Applicant argues that the presently claimed method, as amended, "is specifically designed to generate and identify SH3 domains that have higher binding affinity than the corresponding wild-type domain" and that "[T]here is no disclosure in Lee et al. of obtaining SH3 domains having unnaturally high binding affinities". Applicant's arguments were considered but deemed nonpersuasive for the following reasons.

As discussed in the rejection above, Lee et al. discloses a method of producing SH3 domains from the RT-loop region of different SH3 domains (e.g. from different SH3-kinases). Lee produces said SH3 domains by first mutating some residues of the RT-loop of the different SH3 domains, e.g. page 5010, Fig. 4. The "collection" of mutant RT-loop region is obtained from a library of cDNA (e.g. a collection of 2 or more). "DNA fragments encoding" SH3 domains containing a "randomized RT-loop (RRT-SH3 domains)" are taught by the reference e.g.

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by use of cDNA encoding the kinase (e.g. human Hck) and polymerase chain reaction (e.g. amplification using primers) with "cloning" utilizing a "plasmid *vector*" to generate the recombinant library (e.g. see Lee et al. page 5013, right column). The RT-loop mutated region is then affinity purified to identify the mutant RT-loop peptide that binds to the PXXP motif of a ligand (e.g., Nef) with higher specificity and affinity than the corresponding wild -type SH3 domain ; as well as the binding of the other "artificial" (e.g. unnaturally occurring) SH3 domains to their "desired ligands". In this regard the reference discloses "randomized" substitutions (one or a *combination e.g. 2, 3*) of amino acid substitutions within the RT loop, and specifically within non-conserved (e.g. "variable" regions), and *preferably* including one or more substitutions (e.g. within a specific kinase or among a library of kinases) within a span which "*comprise* six amino acids that immediately follow a conserved stretch of amino acids having an ALYDY consensus sequence". (See e.g. Fig. 4 teaching both conserved and non-conserved amino acids of the RT-loop of kinases and Table I teaching the construction of a library (e.g. a collection) of different kinases having "artificial SH3 domains having desired ligand binding properties" "comprising randomized RT-loops" wherein the collection of SH3 domains contain one or more "random" amino acid substitutions that comprise a hexapeptide sequence "that immediately follows a conserved stretch of amino acids having an ALYDY" (e.g. ...(AL) YDY hexapeptide DLS ...). Additionally Lee specifically exemplifies the use of amino acid mutation (e.g. substitution) within the RT-loop of SH3 proteins (e.g. Fyn) to arrive at a mutant which has increased (e.g. "unnaturally

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high”) ligand (e.g. HIV-1 nef) binding affinity as compared to the corresponding wild type SH3 domain.

Applicant argues that [I]n Lee et al. the RT-loop of Fyn-SH3 was modified to resemble the Hck-SH3 (e.g. a priori deliberate replacement with a known amino acid residue); and that Lee et al. does not disclose the generation of randomized new (e.g. unknown) sequences for RT-loop domains, rather they simply replace the RT-loop of Fyn-SH3 with another naturally occurring RT-loop sequence, that of Hck-SH3.” In fact, according to applicant “Lee et al. may be described as a domain mapping study i.e. a study to determine the importance of particular amino acids in the Nef/kinase binding interaction” (citing the Declaration of Dr. Saksela).

This argument is not found persuasive for several reasons.

Applicant’s attempt to limit the Lee et al. reference to the narrowest possible interpretation of one of its examples (e.g. Hck/Fyn mutant binding study to HIV-1 Nef) fails to appreciate the Lee et al. Reference teaching as a whole to one of ordinary skill in the art.

First, the Lee et al. reference is not limited to one mutant SH3 domain (e.g. the Fyn SH3 mutant referred to by applicant) but extends to the making of multiple SH3 kinase domains containing multiple mutant RT-loop w/n non-conserved regions.

Secondly, the making of a mutant SH3 which *differs from the wild SH3 region* of a kinase would constitute a “new sequence” for one or more RT-loop domains as taught by the reference.

Thirdly, as pointed out in the 102/103 rejection above, the Lee reference clearly teaches (e.g. through example) and suggests (e.g. through explicit statements: e.g. see abstract) the

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making of artificial (e.g. differing from the wild type) SH3 domains of different kinase that contain random (e.g. one or more amino acid substitutions) within the non-conserved regions (particularly a hexapeptide region) of the RT-loop region.

Applicant argue (citing specification discussion on page 4 and 5, lines 6-21) that “the present inventors have found that by using the presently recited method of random generation of the RT-loop sequence combined with affinity selection, instead of merely mimicking known SH3 domains, one can generate SH3 domains with specifically desired binding properties, such as unnaturally high affinity for specific proteins. Applicant further argues that there is no disclosure or suggestion in Lee et al. of a means of generating any but naturally occurring SH3 binding domains or of a method of generating artificial SH3 domains having desired binding properties.

Applicant’s argument is not persuasive since it fails to appreciate both the specific teaching of the Lee et al. reference (through its examples) and the Lee reference teaching taken as a whole. As recited in the 102/103 rejection, the Lee et al. reference provides means for making SH3 domains (e.g. recombinant libraries employing cDNA, PCR, mutagenesis and recombinant libraries using plasmid cloning) and screening for desired (e.g. ligand- binding) clones; which SH3 domains are “artificial” by differing from the wild type due by one or more amino acid substitutions in the non-conserved portion (e.g. variable region) of the RT loop for one or more SH3 kinases.

Dr. Saksela’s statements in the declaration regarding the Lee et al. reference teaching were considered but deemed nonpersuasive for the following reasons. In Dr. Saksela’s opinion, the Lee

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reference failed to “hint that an artificial SH3 domain able to bind to HIV Nef could be made by any other way than mimicking the RT-loop sequence of the Hck tyrosine kinase”. In contrast Dr. Saksela states that “the present invention *discloses* (emphasis provide) that specific binding to HIV Nef can be achieved by combinations of six RT-loop amino acids that bear no similarity whatsoever with the corresponding sequence in Hck or in any other natural SH3 domain”. Applicant further argues that the making/screening of “improved” RT-loop mutants was an unappreciated concept of the Lee reference.

However, to the extent that Dr. Saksela’s arguments address limitations not present in the claim (binding to HIV Nef, combinations of six RT-loop amino acids etc.) this argument is simply not persuasive. Additionally, Dr. Saksela focuses on the specific Lee example, which fails to consider other portions of the Lee et al. document (e.g. Dr. Saksela fails to consider the reference teaching as a whole to one of ordinary skill in the art) pointed to in the rejection regarding the concept of making artificial loop mutants with improved binding characteristics as discussed above. Further, Dr. Saksela’s statement regarding the Lee et al. examples strategy of “mimicking nature” fails to address the fact that the reference teaches the making of “artificial” SH3 domains (e.g. artificial sequences which do not naturally occur) by “randomization” (e.g. the creation of artificial peptides having one or more amino acid substitutions)..

Accordingly, the above revised 102/103 rejection, as modified, is hereby maintained.

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2. Claims 1-4 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. Embo J. Vol. 14, No. 20 pages 5006-5015 (1995) and Sparks et al. J. Biol. Chem. Vol. 269, No. 39 (9/1994) pages 23853-23856.

Lee et al. discloses a method of producing SH3 domains from the RT-loop region of different SH3 domains (e.g. from different SH3-kinases). Lee produces said SH3 domains by first mutating some residues of the RT-loop of the different SH3 domains, e.g. page 5010, Fig. 4. The "collection" of mutant RT-loop region is obtained from a library of cDNA (e.g. a collection of 2 or more). "DNA fragments encoding" SH3 domains containing a "randomized RT-loop (RRT-SH3 domains)" are taught by the reference e.g. by use of cDNA encoding the kinase (e.g. human Hck) and polymerase chain reaction (e.g. amplification using primers) with "cloning" utilizing a "plasmid vector" to generate the recombinant library (e.g. see Lee et al. page 5013, right column). The RT-loop mutated region is then affinity purified to identify the mutant RT-loop peptide that binds to the PXXP motif of a ligand (e.g., Nef) *with higher specificity and affinity* than the corresponding wild -type SH3 domain; as well as the binding of the other "artificial" (e.g. unnaturally occurring) SH3 domains to their "desired ligands". In this regard the reference discloses "randomized" substitutions (one or a *combination e.g. 2, 3*) of amino acid substitutions within the RT loop, and specifically within non-conserved (e.g. "variable" regions), and *preferably* including one or more substitutions (e.g. within a specific kinase or among a library of kinases) within a span which "*comprise* six amino acids that immediately follow a conserved stretch of amino acids having an ALYDY consensus sequence". [See e.g. Fig. 4

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teaching both conserved and non-conserved amino acids of the RT-loop of kinases and Table I teaching the construction of a library (e.g. a collection) of different kinases having "artificial SH3 domains having desired ligand binding properties" "comprising randomized RT-loops" wherein the collection of SH3 domains contain one or more "random" amino acid substitutions that comprise a hexapeptide sequence "that immediately follows a conserved stretch of amino acids having an ALYDY" (e.g. ...**(AL) YDY** hexapeptide DLS ...]. With respect to SH3 binding and specificity (e.g. w/r to differential binding of SH3 containing kinases e.g. Hck and Fyn) to HIV-I, the Lee reference teaches that **"distinct specificity lies in a variable loop, the 'RT loop', positioned close to conserved SH3 residues implicated in the binding of proline-rich (PXXP) motifs" (emphasis provided)**. See ABSTRACT. It is considered that the different mutations of the different SH3 regions of the different kinases is the same to the claimed randomized RT-loop domains or would have been obvious to make into a random collections in view of the Lee's disclosure as to the different amino acids that can be mutated in the different SH3 domains of the SH3 wild type, particularly within the non-conserved regions of the RT-loop motif.

The Lee et al. reference teaching differs from the presently claimed invention (e.g. new claims 17-19) since it fails to explicitly teach generating "artificial Hck-SH3" libraries by randomizing (e.g. with all 20 natural amino acids) the non-conserved hexapeptide 69-74 (EAIHHE) RT-loop sequence of Hck (or related SH3 kinases) to obtain completely random libraries comprising 20^6 (e.g. $20 \times 20 \times 20 \times 20 \times 20 \times 20$) artificial Hck-SH3 proteins differing from the

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wild type at hexapeptide 69-74 (EAIHHE) for subsequent ligand screening (e.g. with HIV-I Nef) and selection of artificial Hck-SH3 proteins containing "optimum" motifs.

However, the Lee et al. reference further teaches that HIV-I Nef protein binds to the SH3 domains of a subset of Src family kinases (including Hck and Fyn); and the SH3 binding capacity of Nef is necessary for optimal spread of HIV-I infection (e.g. via replication). Accordingly, blocking the interaction (e.g. via use of competitive inhibitors) between the HIV-Nef protein and the Src family kinases (e.g. Hck and Fyn) may be therapeutic for HIV infection. See e.g. page 5006 right column to page 5007. The Lee et al. reference further teaches that, w/r to specificity and binding of HIV-I Nef protein to the SH3 domain of Src family kinases, "distinct specificity lies in a variable loop, the 'RT loop', positioned close to conserved SH3 residues implicated in the binding of proline-rich (PXXP) motifs" e.g. at hexapeptide 69-74 (EAIHHE) non-conserved peptide region of Hck (and the corresponding position w/r to the other Src family kinases); and thus the development of artificial SH3 protein analogs which preferentially bind the HIV-I Nef protein may be therapeutic in preventing HIV infection. E. g. See abstract; and page 5013.

Accordingly, the Lee et al. reference provides motivation to one of ordinary skill in the art to make recombinant libraries (using the Lee reference method) that comprise randomization of the non-conserved (e.g. variable) RT loop hexapeptide 69-74 (EAIHHE) peptide sequence of Hck or the corresponding region in other Src family kinases in order to screen such libraries for potential competitive inhibitors useful in treating HIV infection.

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One would be motivated to completely randomize the hexapeptide variable RT loop region in order to obtain the largest possible library (e.g. a completely random library comprising 20^6 (e.g. $20 \times 20 \times 20 \times 20 \times 20 \times 20$) artificial Hck-SH3 proteins or other artificial Src family kinase proteins) for screening and thus *optimizing* the likelihood of finding therapeutically useful competitive inhibitors.

Thus, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention, in light of the Lee reference teaching alone, to generate "artificial Hck-SH3" peptide (or other Src family kinase peptide) libraries by randomizing (e.g. with all 20 natural amino acids) a hexapeptide 69-74 (EAIHHE) of Hck (or the corresponding region of a related Src family protease) to obtain a complete random library comprising 20^6 artificial Hck-SH3 proteins differing from the wild type at hexapeptide 69-74 (EAIHHE) since the Lee reference suggests the making of competitive inhibitors of HIV infection by modifying the amino acids in the variable hexapeptide (69-74) region of Hck (or other Src family kinases) to generate inhibitors. Additionally, the making of the largest library (e.g by complete randomization of each amino acid) for screening potential HIV-I inhibitors represents mere optimization.

Additionally, the Sparks et al. reference teaches the utilization of "biased peptide libraries" or , preferentially "random peptide libraries" (e.g. all 20 amino acids), including 7mer/8mer peptide libraries, via phage display, as a means for making and screening Src SH3 **high-affinity** peptide ligands for developing "antagonists of Src SH3 interactions with SH3-binding proteins" . See abstract; and entire article.

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Accordingly, the Sparks et al. reference provides further motivation to make and screen "random peptide libraries" for developing "antagonists of Src SH3 interactions with SH3-binding proteins" which can be useful to treat HIV infection.

Thus, it would have been obvious to one of ordinary skill in the art, in view of the combined teaching of the Lee and Sparks references, to generate "artificial Hck-SH3" (or other Src family kinase proteins) libraries by making "random peptide libraries" comprising the hexapeptide 69-74 (EAIHHE) peptide sequence (or corresponding sequence) to obtain a complete random library, using either the Lee (recombinant) or Sparks (phage display) method of library generation in order to screen for potential HIV therapeutics.

Discussion

Applicant's arguments directed against the above obviousness rejection were considered but deemed nonpersuasive for the following reasons. Initially, it is noted that the above rejection was modified in response to applicant's claim amendment(s) and arguments already addressed by the Examiner above will not be reiterated here.

Applicant argues that neither that the Lee et al. And Sparks et al. references were addressing a "domain mapping study" and not the generation of SH3 domains having higher than natural binding affinity. This argument was considered but deemed nonpersuasive for the same reasons recited in the above 102/103 rejection over the Lee et al. reference all of which are specifically incorporated by reference in its entirety. In summary, Lee et al. teaches the (recombinant) making and screening of mutant RT-loop libraries which bind to the PXXP motif of

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a ligand (e.g., Nef) with higher specificity and affinity than the corresponding wild -type SH3 domain ; as well as the binding of the other “artificial” (e.g. unnaturally occurring) SH3 domains to their “desired ligands”.

Regarding applicant’s assertion that the Sparks et al. reference is strictly an exercise in epitope mapping, clearly mischaracterizes the Sparks et al. Reference teaching which screens random libraries and obtains “high affinity peptide ligands” (e.g. see abstract).

To the extent that Applicant argues that the Sparks et al. Reference addresses the PXXP motif (e.g. of the ligand) which differs from the presently claimed emphasis on the SH3 domain (e.g. of the enzyme receptor), this argument is not persuasive since applicant's arguments against the Sparks e al. references individually, cannot show nonobviousness where the rejection is based on a combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Accordingly, the above modified rejection is hereby maintained.

New Objection (s) and/or Rejection (s)

Claim Objections

3. Claim 1 is objected to because of the following informalities: reciting “containing a randomized mutations...”. Appropriate correction is required.
4. Claims 1-4 and 17-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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In claim 1 (and claims dependent thereon), the phrase “ligand binding affinity that is higher than the affinity of corresponding wild-type SH3 domain” and “selecting domains with a binding affinity that is higher than the binding affinity of the corresponding wild-type SH3 domain” is indefinite as to what the standard “ligand” and the standard “wild-type SH2 domain” is for means of comparison regarding binding affinity.

5. Claims 1-4 and 17-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (e.g. NEW MATTER REJECTION) .

In claim 1 (and claims dependent thereon), the newly amended claims containing the phrase “ligand binding affinity that is higher than the affinity of corresponding wild-type SH3 domain” and the phrase “selecting domains with a binding affinity that is higher than the binding affinity of the corresponding wild-type SH3 domain” constitutes new matter since there is no direct specification support for the newly added claim language nor has applicant indicated where such support exists. The specification merely provides support (E.g. pages 6-7) for the screening of mutant HckSH3 library proteins that have higher binding affinity to the HckSH3 cognate ligand (e.g. HIV-1Nef) wherein the mutant Hck SH3 library proteins are formed from *randomization (e.g. with 20 natural amino acids) of a six amino acid variable RT-loop* (immediately following seq. Id 1).

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6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang (art unit 1639), can be reached at (703)306-3217.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1639)

August 25, 2003

BENNETT CELSA
PRIMARY EXAMINER

